

**Supplementary table S1 Association analysis of the human KLK region polymorphism with SLE and lupus nephritis.**

Chr.	SNP	BP Position	Gene	Allele	Frequency Cases	Frequency Controls	SLE vs. controls <sup>1</sup>				SLE Nephritis vs. controls <sup>1,2</sup>			
							OR	L95	U95	P-value	OR	L95	U95	P-value
19	rs5519	56014125	<i>KLK1</i>	C	0.27	0.26	1.04	0.93	1.16	0.51	1.01	0.84	1.22	0.92
19	rs266850	56028010		G	0.17	0.19	0.85	0.75	0.97	<b>0.01312</b>	0.79	0.63	0.99	<b>0.0388</b>
19	rs266851	56028152		T	0.20	0.18	1.11	0.99	1.26	0.08	1.02	0.83	1.26	0.83
19	rs266858	56031775		C	0.22	0.26	0.83	0.74	0.93	<b>0.0009081</b>	0.88	0.73	1.07	0.19
19	rs2569729	56037634		A	0.19	0.18	1.10	0.97	1.24	0.14	1.08	0.88	1.34	0.45
19	rs266849	56040903		G	0.19	0.20	0.92	0.82	1.04	0.17	0.96	0.79	1.18	0.73
19	rs266870	56043747		C	0.50	0.49	1.01	0.92	1.12	0.77	1.01	0.85	1.19	0.93
19	rs266868	56044750		A	0.30	0.30	0.97	0.87	1.08	0.57	1.01	0.84	1.21	0.93
19	rs3760722	56049629	<i>KLK3</i>	T	0.10	0.10	1.06	0.90	1.24	0.49	1.16	0.89	1.51	0.27
19	rs1058205	56055211	<i>KLK3</i>	C	0.17	0.19	0.92	0.81	1.04	0.16	0.93	0.75	1.15	0.52
19	rs2735839	56056436		A	0.14	0.15	0.95	0.83	1.08	0.41	0.97	0.77	1.22	0.78
19	rs1506684	56063232		A	0.46	0.46	1.03	0.94	1.13	0.52	1.07	0.91	1.26	0.39
19	rs198972	56071706	<i>KLK2</i>	T	0.32	0.31	1.03	0.93	1.14	0.63	1.10	0.93	1.31	0.27
19	rs198979	56075993	<i>KLK2</i>	C	0.10	0.10	1.11	0.95	1.30	0.20	0.98	0.73	1.31	0.89
19	rs2664144	56083469		C	0.10	0.10	1.07	0.92	1.25	0.37	0.98	0.75	1.29	0.89
19	rs1354774	56084931		G	0.37	0.37	1.00	0.91	1.11	0.99	1.06	0.89	1.25	0.53
19	rs2235091	56102284	<i>KLK4</i>	G	0.37	0.37	1.01	0.92	1.12	0.78	1.02	0.86	1.21	0.82
19	rs2242670	56104128	<i>KLK4</i>	A	0.46	0.44	1.11	1.00	1.22	<b>0.04103</b>	1.17	0.99	1.38	0.06
19	rs7248321	56110318		C	0.05	0.05	0.93	0.75	1.17	0.54	1.04	0.72	1.50	0.85
19	rs1701930	56111359		A	0.41	0.42	0.96	0.87	1.06	0.43	1.09	0.92	1.28	0.32
19	rs268917	56116667		A	0.44	0.45	0.95	0.87	1.05	0.34	1.06	0.89	1.24	0.53
19	rs7245858	56122409	<i>LOC390956</i>	G	0.03	0.03	0.80	0.60	1.06	0.12	0.92	0.58	1.47	0.74
19	rs7255259	56131022	<i>LOC390956</i>	G	0.08	0.08	1.09	0.92	1.30	0.33	1.44	1.10	1.88	<b>0.008607</b>
19	rs8104441	56133620		C	0.18	0.18	1.05	0.93	1.19	0.42	0.90	0.72	1.12	0.35
19	rs268914	56134512		G	0.32	0.33	0.96	0.87	1.06	0.44	1.25	1.06	1.49	<b>0.008991</b>
19	rs268909	56141477	<i>KLK5</i>	G	0.16	0.17	0.97	0.85	1.10	0.66	1.24	1.01	1.53	<b>0.03866</b>
19	rs268905	56142742	<i>KLK5</i>	T	0.28	0.28	1.00	0.90	1.11	0.94	0.91	0.75	1.09	0.30
19	rs4592765	56151844	<i>KLK6</i>	C	0.40	0.39	1.06	0.96	1.17	0.23	1.03	0.87	1.21	0.75
19	rs1654537	56158329	<i>KLK6</i>	G	0.34	0.33	1.01	0.91	1.12	0.85	0.98	0.82	1.17	0.82
19	rs1275221	56178880	<i>KLK7</i>	T	0.36	0.35	1.02	0.92	1.12	0.76	0.85	0.71	1.02	0.07
19	rs268899	56183902		C	0.37	0.36	1.04	0.94	1.15	0.43	1.01	0.86	1.20	0.87
19	rs1654543	56190802	<i>KLK8</i>	C	0.45	0.45	1.01	0.92	1.11	0.88	0.91	0.77	1.07	0.26
19	rs2569456	56197538	<i>KLK9</i>	A	0.34	0.33	1.07	0.96	1.18	0.21	1.08	0.91	1.28	0.37
19	rs2075695	56210110	<i>KLK10</i>	A	0.44	0.44	0.98	0.89	1.08	0.63	1.05	0.89	1.24	0.55
19	rs2691208	56217901	<i>KLK11</i>	A	0.16	0.17	0.90	0.79	1.02	0.10	0.86	0.68	1.08	0.19
19	rs1048328	56219177	<i>KLK11</i>	A	0.10	0.09	1.10	0.93	1.30	0.27	1.24	0.94	1.64	0.13
19	rs3745539	56219854	<i>KLK11</i>	T	0.07	0.08	0.86	0.72	1.04	0.12	0.57	0.39	0.84	<b>0.004004</b>
19	rs2250066	56220932	<i>KLK11</i>	T	0.15	0.13	1.13	0.99	1.30	0.08	1.00	0.79	1.27	1.00
19	rs3745540	56226943	<i>KLK12</i>	A	0.43	0.42	1.03	0.93	1.13	0.59	1.03	0.87	1.21	0.77
19	rs3865443	56229495	<i>KLK12</i>	A	0.23	0.25	0.89	0.80	0.99	<b>0.04048</b>	1.07	0.89	1.29	0.47
19	rs3760739	56230374	<i>KLK12</i>	T	0.35	0.33	1.06	0.96	1.17	0.26	1.00	0.84	1.19	0.99
19	rs2691229	56238455		C	0.49	0.49	1.03	0.94	1.13	0.54	0.95	0.80	1.12	0.51
19	rs2569469	56241011		A	0.31	0.30	1.08	0.98	1.20	0.12	1.08	0.90	1.28	0.42
19	rs2691239	56243625		A	0.36	0.38	0.91	0.82	1.00	<b>0.04669</b>	0.95	0.80	1.12	0.54
19	rs1880413	56252280	<i>KLK13</i>	C	0.33	0.34	0.94	0.85	1.04	0.21	0.95	0.80	1.13	0.56
19	rs8111658	56252836	<i>KLK13</i>	C	0.36	0.37	0.99	0.90	1.10	0.90	0.93	0.78	1.10	0.39
19	rs1001538	56263968		C	0.28	0.29	0.91	0.82	1.01	0.07	0.91	0.76	1.09	0.32
19	rs2569481	56267237		A	0.28	0.29	0.94	0.84	1.04	0.23	0.95	0.79	1.14	0.58
19	rs2569484	56268087		T	0.28	0.29	0.94	0.85	1.05	0.27	0.96	0.80	1.15	0.68
19	rs2569488	56271459	<i>KLK14</i>	C	0.35	0.37	0.92	0.84	1.02	0.11	0.95	0.81	1.13	0.59
19	rs867191	56275429	<i>KLK14</i>	C	0.06	0.06	1.03	0.85	1.25	0.74	0.98	0.70	1.38	0.91
19	rs9304708	56275749	<i>KLK14</i>	T	0.34	0.36	0.93	0.85	1.03	0.18	0.96	0.81	1.14	0.67
19	rs17658926	56276223	<i>KLK14</i>	A	0.20	0.19	0.99	0.88	1.11	0.85	1.05	0.85	1.28	0.67
19	rs10500304	56276411	<i>KLK14</i>	G	0.39	0.41	0.93	0.84	1.02	0.11	0.95	0.81	1.13	0.58
19	rs2569491	56276729	<i>KLK14</i>	A	0.33	0.34	0.94	0.85	1.04	0.22	0.99	0.84	1.18	0.92
19	rs2072689	56277428	<i>KLK14</i>	T	0.47	0.48	0.96	0.88	1.06	0.44	1.03	0.88	1.21	0.73

<sup>1</sup> The association analysis was performed by logistic regression and adjusted by gender introducing it as a covariable in the regression model. <sup>2</sup> Only the patients with nephritis were considered as cases. OR: odds ratio, L95: lower limit of the 95% confidence interval, U95: upper limit of the 95% confidence interval.

**Supplementary table S2 Case-only meta-analysis of the human KLK region polymorphism comparing SLE cases with nephritis to SLE cases without nephritis.**

CHR	SNP	Base pair position	Gene	A1	Frequency in cases with nephritis	Frequency in cases without nephritis	P <sub>CMH</sub>	OR	L95	U95	P <sub>HOMO</sub>
19	rs5519	56014125	<i>KLK1</i>	C	0.26	0.27	0.82	0.98	0.79	1.21	0.20
19	rs266850	56028010		G	0.16	0.17	0.28	0.87	0.67	1.13	0.45
19	rs266851	56028152		T	0.19	0.20	0.38	0.89	0.70	1.15	0.83
19	rs266858	56031775		C	0.24	0.22	0.40	1.10	0.88	1.39	0.56
19	rs2569729	56037634		A	0.19	0.19	0.93	0.99	0.77	1.27	0.70
19	rs266849	56040903		G	0.20	0.20	0.66	1.06	0.83	1.34	0.60
19	rs266870	56043747		C	0.49	0.50	0.56	0.94	0.78	1.15	0.84
19	rs266868	56044750		A	0.31	0.29	0.56	1.06	0.86	1.31	0.78
19	rs3760722	56049629	<i>KLK3</i>	T	0.11	0.10	0.29	1.18	0.87	1.60	0.28
19	rs1058205	56055211	<i>KLK3</i>	C	0.18	0.18	0.91	1.02	0.79	1.31	0.44
19	rs2735839	56056436		A	0.15	0.14	0.74	1.05	0.80	1.37	0.26
19	rs1506684	56063232		A	0.47	0.46	0.25	1.12	0.92	1.37	0.99
19	rs198972	56071706	<i>KLK2</i>	T	0.33	0.32	0.36	1.10	0.90	1.35	0.20
19	rs198979	56075993	<i>KLK2</i>	C	0.09	0.11	0.28	0.83	0.59	1.16	0.33
19	rs2664144	56083469		C	0.10	0.11	0.38	0.87	0.63	1.20	0.21
19	rs1354774	56084931		G	0.38	0.36	0.38	1.09	0.90	1.34	0.40
19	rs2235091	56102284	<i>KLK4</i>	G	0.38	0.37	0.97	1.00	0.82	1.23	0.68
19	rs2242670	56104128	<i>KLK4</i>	A	0.48	0.45	0.23	1.13	0.93	1.37	0.49
19	rs7248321	56110318		C	0.05	0.04	0.25	1.30	0.83	2.04	0.30
19	rs1701930	56111359		A	0.44	0.40	<b>0.03345</b>	1.24	1.02	1.50	0.89
19	rs268917	56116667		A	0.47	0.42	0.07	1.20	0.99	1.45	0.73
19	rs7245858	56122409	<i>LOC390956</i>	G	0.03	0.02	0.25	1.40	0.79	2.50	0.41
19	rs7255259	56131022	<i>LOC390956</i>	G	0.11	0.08	<b>0.001313</b>	1.67	1.22	2.30	0.30
19	rs8104441	56133620		C	0.16	0.19	0.12	0.81	0.63	1.05	0.22
19	rs268914	56134512		G	0.39	0.30	<b>1.36E-05</b>	1.56	1.28	1.91	0.50
19	rs268909	56141477	<i>KLK5</i>	G	0.20	0.15	<b>0.0007579</b>	1.53	1.19	1.96	0.55
19	rs268905	56142742	<i>KLK5</i>	T	0.26	0.29	0.14	0.85	0.68	1.06	0.72
19	rs4592765	56151844	<i>KLK6</i>	C	0.39	0.40	0.84	0.98	0.80	1.19	0.58
19	rs1654537	56158329	<i>KLK6</i>	G	0.33	0.34	0.47	0.93	0.75	1.14	0.94
19	rs1275221	56178880	<i>KLK7</i>	T	0.32	0.37	<b>0.02725</b>	0.79	0.64	0.97	0.71
19	rs268899	56183902		C	0.37	0.37	0.31	0.90	0.74	1.10	0.99
19	rs1654543	56190802	<i>KLK8</i>	C	0.42	0.46	0.05	0.82	0.68	1.00	0.99
19	rs2569456	56197538	<i>KLK9</i>	A	0.35	0.34	0.55	0.94	0.76	1.16	0.94
19	rs2075695	56210110	<i>KLK10</i>	A	0.46	0.44	0.28	1.11	0.92	1.35	1.00
19	rs2691208	56217901	<i>KLK11</i>	A	0.15	0.16	0.19	0.83	0.63	1.09	0.68
19	rs1048328	56219177	<i>KLK11</i>	A	0.11	0.09	0.10	1.31	0.95	1.81	0.34
19	rs3745539	56219854	<i>KLK11</i>	T	0.05	0.08	<b>0.01117</b>	0.57	0.37	0.88	0.45
19	rs2250066	56220932	<i>KLK11</i>	T	0.13	0.16	0.23	0.84	0.63	1.12	0.12
19	rs3745540	56226943	<i>KLK12</i>	A	0.43	0.43	0.49	0.93	0.77	1.14	0.14
19	rs3865443	56229495	<i>KLK12</i>	A	0.27	0.22	<b>0.008919</b>	1.34	1.08	1.67	0.22
19	rs3760739	56230374	<i>KLK12</i>	T	0.33	0.35	0.35	0.91	0.74	1.11	0.98
19	rs2691229	56238455		C	0.47	0.50	0.40	0.92	0.76	1.12	0.60
19	rs2569469	56241011		A	0.31	0.30	0.74	1.04	0.84	1.28	0.79
19	rs2691239	56243625		A	0.37	0.36	0.60	1.06	0.86	1.29	0.48
19	rs1880413	56252280	<i>KLK13</i>	C	0.33	0.34	0.76	1.03	0.84	1.27	0.91

19	rs8111658	56252836	<i>KLK13</i>	C	0.35	0.36	0.43	0.92	0.75	1.13	0.34
19	rs1001538	56263968		C	0.27	0.28	0.67	0.95	0.77	1.19	0.25
19	rs2569481	56267237		A	0.28	0.27	0.73	1.04	0.84	1.29	0.25
19	rs2569484	56268087		T	0.28	0.27	0.65	1.05	0.85	1.31	0.23
19	rs2569488	56271459	<i>KLK14</i>	C	0.36	0.35	0.72	1.04	0.85	1.27	0.82
19	rs867191	56275429	<i>KLK14</i>	C	0.06	0.06	0.94	0.99	0.66	1.47	0.39
19	rs9304708	56275749	<i>KLK14</i>	T	0.35	0.34	0.94	1.01	0.82	1.24	0.77
19	rs17658926	56276223	<i>KLK14</i>	A	0.20	0.20	0.98	1.00	0.78	1.27	0.35
19	rs10500304	56276411	<i>KLK14</i>	G	0.40	0.39	0.95	0.99	0.82	1.21	0.77
19	rs2569491	56276729	<i>KLK14</i>	A	0.34	0.33	0.67	1.05	0.85	1.28	0.63
19	rs2072689	56277428	<i>KLK14</i>	T	0.48	0.47	0.23	1.13	0.93	1.37	0.75

P<sub>CMH</sub>: P-value from the Cochran-Mantel-Haenzel meta-analysis performed within cases, which takes into account the variability across the different strata, in this, cases the patient's clinical center. P<sub>HOMOG</sub>: P value for the homogeneity test between strata. The non-significant results indicate homogeneity of the association. OR: odds ratio, L95: lower limit of the 95% confidence interval, U95: upper limit of the 95% confidence interval.

**Supplementary table S3 Haplotypic association analyses.**

Haplotype block	Haplotype	Freq controls	Freq SLE	Freq SLE nephritis	Frequency SLE no nephritis	SLE vs. controls	SLE nephritis vs. controls	SLE nephritis vs. SLE no nephritis	P-value	P-value	P-value
Block 1	OMNIBUS	--	--	--	--	0.0008359	0.2641	0.318			
	GCC	0.18	0.16	0.15	0.16	<b>0.009036*</b>	<b>0.06646</b>	0.6231			
	ACC	0.08	0.06	0.08	0.06	<b>0.01237</b>	0.7238	0.1637			
	ATT	0.18	0.20	0.18	0.20	<b>0.02412</b>	0.9759	0.2034			
	ACT	0.56	0.58	0.60	0.58	0.115	0.1131	0.489			
Block 2	OMNIBUS	--	--	--	--	0.2897	0.8511	0.8611			
	GACA	0.28	0.27	0.28	0.27	0.6126	0.794	0.4326			
	GACG	0.23	0.24	0.23	0.25	0.4375	0.7119	0.3049			
	GGTG	0.19	0.19	0.19	0.19	0.3454	0.869	0.8013			
	AATG	0.18	0.20	0.20	0.19	0.09253	0.3676	0.992			
	GATG	0.11	0.11	0.10	0.11	0.2257	0.4436	0.967			
Block 3	OMNIBUS	--	--	--	--	0.5282	0.4745	0.6379			
	CCA	0.16	0.15	0.15	0.15	0.357	0.6816	0.9143			
	TTG	0.10	0.11	0.12	0.10	0.4353	0.2312	0.3592			
	CTG	0.74	0.75	0.73	0.75	0.8248	0.6258	0.4618			
Block 4	OMNIBUS	--	--	--	--	0.4984	0.5133	0.3443			
	TCCG	0.09	0.09	0.08	0.10	0.5916	0.5884	0.2564			
	TTTG	0.20	0.20	0.22	0.19	0.9226	0.1862	0.1179			
	CTTG	0.09	0.08	0.08	0.08	0.1426	0.4167	0.8718			
	CTTA	0.62	0.63	0.61	0.63	0.5391	0.7646	0.4857			
Block 5	OMNIBUS	--	--	--	--	0.2724	0.6005	<b>0.04465</b>			
	TAAA	0.40	0.38	0.42	0.36	0.2038	0.3162	<b>0.01417</b>			
	TAGA	0.07	0.08	0.07	0.08	0.2103	0.9174	0.3207			
	TGGA	0.53	0.54	0.51	0.56	0.5518	0.3521	0.06413			
Block 6	OMNIBUS	--	--	--	--	0.5431	<b>0.03104</b>	<b>0.001309</b>			
	GTGG	0.08	0.08	0.11	0.08	0.5427	<b>0.00764</b>	<b>0.006601</b>			
	ATGG	0.06	0.06	0.06	0.05	0.2113	0.9355	0.2056			
	ATGA	0.20	0.19	0.22	0.18	0.4235	0.171	<b>0.02579</b>			
	ACAA	0.18	0.18	0.16	0.19	0.3388	0.3489	0.1123			
	ATAA	0.48	0.48	0.44	0.50	0.8665	0.05769	<b>0.008754</b>			
Block 7	OMNIBUS	--	--	--	--	0.2005	<b>0.02015</b>	0.05108			
	CCA	0.32	0.33	0.34	0.32	0.1611	0.2937	0.6253			
	CCC	0.05	0.05	0.04	0.05	0.2258	0.05225	0.08427			
	ACC	0.09	0.08	0.06	0.09	0.1487	<b>0.02109</b>	<b>0.04002</b>			
	ATC	0.54	0.54	0.57	0.54	0.9702	0.2381	0.1626			
Block 8	OMNIBUS	--	--	--	--	0.1044	<b>0.002529</b>	<b>0.01334</b>			
	AGGT	<b>0.07</b>	<b>0.06</b>	<b>0.04</b>	0.07	<b>0.02648</b>	<b>0.001114*</b>	<b>0.004292</b>			
	GGAC	0.08	0.09	0.10	0.09	0.3057	0.1566	0.2941			
	GAGC	0.17	0.16	0.15	0.16	0.2169	0.3436	0.5861			
	AGGC	0.37	0.37	0.41	0.36	0.5268	<b>0.01757</b>	<b>0.0282</b>			
	GGGC	0.31	0.32	0.29	0.32	0.3459	0.4491	0.3068			
Block 9	OMNIBUS	--	--	--	--	0.4908	0.9606	0.3975			
	GCTC	0.36	0.37	0.35	0.37	0.4104	0.8801	0.5035			
	ACGC	0.13	0.13	0.13	0.13	0.9692	0.7942	0.7553			
	GAGT	0.23	0.21	0.24	0.20	0.1277	0.6014	0.08535			
	ACGT	0.29	0.29	0.28	0.30	0.615	0.8944	0.5415			
Block 10	OMNIBUS	--	--	--	--	0.5014	0.3786	0.7334			
	TC	0.37	0.36	0.35	0.36	0.8415	0.3604	0.5546			
	CT	0.34	0.33	0.33	0.34	0.388	0.7012	0.8981			
	TT	0.29	0.30	0.32	0.30	0.2685	0.1723	0.4562			
Block 11	AT	0.29	0.28	0.28	0.27	0.2701	0.6023	0.7			
	GG	0.71	0.72	0.72	0.73	0.2701	0.6023	0.7			
Block 12	OMNIBUS	--	--	--	--	0.3867	0.7956	0.9749			
	CTTAGA	0.21	0.21	0.22	0.21	0.897	0.6123	0.6668			
	CTTGGA	0.15	0.14	0.14	0.14	0.0956	0.3428	0.9346			
	TCGGTG	0.07	0.07	0.07	0.07	0.7415	0.9105	0.9249			
	TTGGTG	0.57	0.58	0.58	0.58	0.2563	0.746	0.7134			

The linkage disequilibrium structure of the region showed 12 haplotype blocks (see figure 6A). These blocks were tested for haplotype association by both omnibus and haplotype-specific association statistics (T test) as implemented in PLINK. The case/control omnibus test is an H-1 degree of freedom test, if there are H haplotypes. The two most significant associations (\*) correspond to haplotypes with a lower frequency in patients, even less in the subgroup of patients with nephritis, reflecting a protective effect conferred by the KLK polymorphisms